Amendment to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Currently amended) A conjugate for use in targeting a drug to a tissue, wherein a digestive enzyme is overexpressed in the extracellular space of the tissue, the conjugate comprising:

a polymeric carrier;

a drug molecule; and

a linker that includes a first end and a second end[[,]]; wherein the polymeric carrier is associated with the first end of the linker and the drug is associated with the second end of the linker; ~~and~~ wherein the linker includes an oligopeptide recognition segment that is cleaved when the conjugate is exposed to the digestive enzyme; and wherein the digestive enzyme is selected from the group consisting of serine proteases and matrix metalloproteinases.

2. (Currently amended) The conjugate of claim 1 further comprising:

additional drug molecules; and

additional linkers, wherein each drug molecule is indirectly associated with the polymeric carrier via one of the linkers and wherein each linker includes an oligopeptide recognition segment that is cleaved when the conjugate is exposed to the digestive enzyme.

3. (Original) The conjugate of claim 1, wherein the polymeric carrier is hydrophilic, biocompatible and biodegradable.

4. (Currently amended) The conjugate of claim 1, wherein the size of the polymeric carrier is larger than the renal excretion limit.

5. (Original) The conjugate of claim 1, wherein the drug is a small molecule drug.

6. (Original) The conjugate of claim 1, wherein the drug is a biomolecular drug.

7. (Canceled)

8. (Canceled)

9. (Original) The conjugate of claim 1, wherein the tissue is diseased.

10. (Original) The conjugate of claim 9, wherein the tissue is a tumor.

11. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of the conjugate of claim 1.

12. (Currently amended) A method of preparing a conjugate for use in targeting a drug to a tissue, wherein the tissue overexpresses a digestive enzyme, the method comprising:

providing a polymer carrier;

providing a drug molecule;

providing a linker that includes at least a first end and a second end, wherein the linker includes an oligopeptide recognition segment that is cleaved when the conjugate is exposed to the digestive enzyme, and the digestive enzyme is selected from the group consisting of serine proteases and matrix metalloproteinases;

associating the polymer carrier with the first end of the linker; and

associating the drug molecule with the second end of the linker.

13. (Currently amended) A method of ~~administering~~ targeting a drug to a tissue in a patient, wherein a digestive enzyme is overexpressed in the extracellular space of the tissue, the method comprising steps of:

providing a patient;

providing a pharmaceutical composition that comprises a pharmaceutically acceptable excipient and an effective amount of ~~the~~ a conjugate ~~of claim 1~~; and

administering the pharmaceutical composition to the patient; wherein the conjugate comprises:

a polymeric carrier;

a drug molecule; and

a linker that includes a first end and a second end; wherein the polymeric carrier is associated with the first end of the linker and the drug is associated with the second end of the linker; wherein the linker includes an oligopeptide recognition segment that is cleaved when the conjugate is exposed to the digestive enzyme; and wherein the digestive enzyme is selected from the group consisting of serine proteases and matrix metalloproteinases.

14. (New) The conjugate of claim 1, wherein the polymeric carrier is dextran.

15. (New) The conjugate of claim 1, wherein the oligopeptide recognition segment comprises the amino acid sequence IPVGLIG.

16. (New) The conjugate of claim 14, wherein the oligopeptide recognition segment comprises the amino acid sequence IPVGLIG.

17. (New) The conjugate of claim 1, wherein the drug is methotrexate.

18. (New) The conjugate of claim 14, wherein the drug is methotrexate.

19. (New) The conjugate of claim 15, wherein the drug is methotrexate.

20. (New) The conjugate of claim 16, wherein the drug is methotrexate.

21. (New) The conjugate of claim 1, wherein the drug is doxorubicin.

22. (New) The conjugate of claim 14, wherein the drug is doxorubicin.

23. (New) The conjugate of claim 22, wherein the oligopeptide recognition segment comprises the amino acid sequence IPVGLIG.

24. (New) The conjugate of claim 1, wherein the digestive enzyme is a serine protease.

25. (New) The conjugate of claim 24, wherein the digestive enzyme is prostate specific antigen (PSA).

26. (New) The conjugate of claim 24, wherein the digestive enzyme is human kallikrein 2 (hk2).

27. (New) The conjugate of claim 24, wherein the digestive enzyme is urokinase-type plasminogen activator (uPA).

28. (New) The conjugate of claim 24, wherein the digestive enzyme is fibroblast activating protein α (FAPα).

29. (New) The conjugate of claim 1, wherein the digestive enzyme is a matrix metalloproteinase.

30. (New) The conjugate of claim 29, wherein the digestive enzyme is Meprin α.

31. (New) The conjugate of claim 29, wherein the digestive enzyme is Meprin β.

32. (New) The conjugate of claim 29, wherein the digestive enzyme is MT1-MMP.

33. (New) The conjugate of claim 29, wherein the digestive enzyme is matrix metalloproteinase II (MMP-2).

34. (New) The method of claim 13, wherein the digestive enzyme is a serine protease

35. (New) The method of claim 34, wherein the digestive enzyme is prostate specific antigen (PSA).

36. (New) The method of claim 34, wherein the digestive enzyme is human kallikrein 2 (hk2).

37. (New) The method of claim 34, wherein the digestive enzyme is urokinase-type plasminogen activator (uPA).

38. (New) The method of claim 34, wherein the digestive enzyme is fibroblast activating protein α (FAPα).

39. (New) The method of claim 13, wherein the digestive enzyme is a matrix metalloproteinase.

40. (New) The method of claim 39, wherein the digestive enzyme is Meprin α.

41. (New) The method of claim 39, wherein the digestive enzyme is Meprin β.

42. (New) The method of claim 39, wherein the digestive enzyme is MT1-MMP.

43. (New) The method of claim 39, wherein the digestive enzyme is matrix metalloproteinase II (MMP-2).

44. (New) The method of claim 13, wherein the polymeric carrier is dextran.

45. (New) The method of claim 13, wherein the oligopeptide recognition segment comprises the amino acid sequence IPVGLIG.

46. (New) The method of claim 44, wherein the oligopeptide recognition segment comprises the amino acid sequence IPVGLIG.

47. (New) The method of claim 13, wherein the drug is methotrexate.

48. (New) The method of claim 44, wherein the drug is methotrexate.

49. (New) The method of claim 45, wherein the drug is methotrexate.

50. (New) The method of claim 46, wherein the drug is methotrexate.

51. (New) The method of claim 13, wherein the drug is doxorubicin.

52. (New) The method of claim 44, wherein the drug is doxorubicin.

53. (New) The method of claim 52, wherein the oligopeptide recognition segment comprises the amino acid sequence IPVGLIG.

54. (New) The method of claim 13, wherein the conjugate is administered in an amount effective to treat an epithelial cancer in the patient.

55. (New) The method of claim 13, wherein the conjugate is administered in an amount effective to treat breast, prostate, bladder, ovarian, bladder, or gastric cancer in the patient.

56. (New) The method of claim 13, wherein the conjugate is administered in an amount effective to treat arthritis in the patient.